

Fusion proteins of protease inhibitors are provided, in particular fusion proteins of alpha 1-antitrypsin (AAT) and a second protease inhibitor, such as secretory leukocyte protease inhibitor (SLPI) or tissue inhibitor of metalloproteases (TIMP). Polynucleotides encoding the fusion proteins, vectors comprising such polynucleotides, and host cells containing such vectors are also provided. Methods of making the fusion proteins of the invention are also provide, as well as methods of using the fusion proteins, for example to inhibit protease activity in a biological sample or in the treatment of an individual suffering from, or at risk for, a disease or disorder involving unwanted protease activity.